

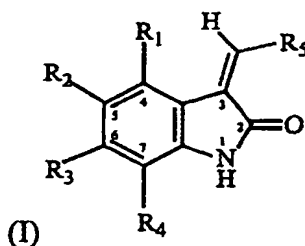
**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

1. (Currently amended) A method of determining an efficacious dose of a compound administered to a subject for the purpose of modulating angiogenesis, comprising the steps of:

(a) administering the compound to a patient, wherein the compound is a receptor antagonist that inhibits a receptor involved in angiogenesis and wherein the compound is an indolinone compound, having the structure set forth in formula I:



wherein

(i) R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, and R<sub>4</sub> are selected from the group consisting of hydrogen, trihalomethyl, hydroxyl, amine, thioether, cyano, alkoxy, alkyl, amino, bromo, fluoro, chloro, iodo, mercapto, thio, cyanoamido, alkylthio, aryl, heteroaryl, carboxyl, ester, oxo, alkoxycarbonyl, alkenyl, alkoxy, nitro, alkoxyl, and amido moieties; and

(ii) R<sub>5</sub>, is an optionally substituted aryl or heteroaryl cyclic moiety;

or a pharmaceutically acceptable salt, ester, amide, prodrug, isomer, or metabolite thereof;

(b) monitoring the release of a marker selected from the group consisting of tissue factor, CD40, u-PA, ETS-1, IL8, and t-PA;

(c) constructing a standard curve which provides the relationship between the amount of said marker released per a known number of cells as a function of the dose of a compound of the formula I; and

(d) determining the efficacious dose based on the standard curve by determining the ratio of the amount of said marker to the dose of the administered compound of the formula I.

2. (Original) The method of claim 1, wherein said angiogenesis is modulated to treat or prevent conditions associated with angiogenesis including conditions manifested by cell proliferation, cell differentiation, or cell survival.

3. (Original) The method of claim 2, wherein said conditions associated with cell proliferation is selected from the group consisting of cancer, arthritis, endometriosis, and ocular neovascularization.

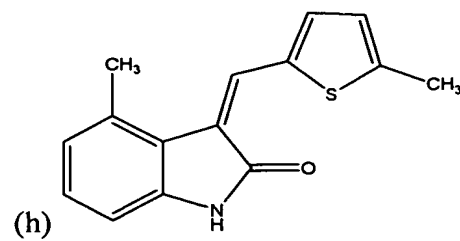
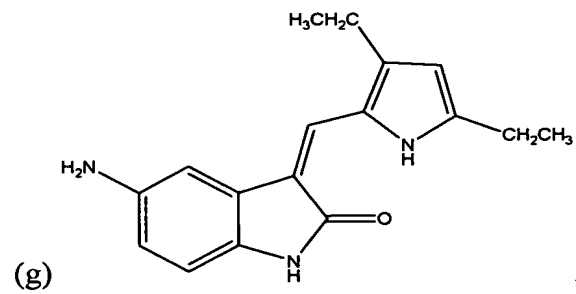
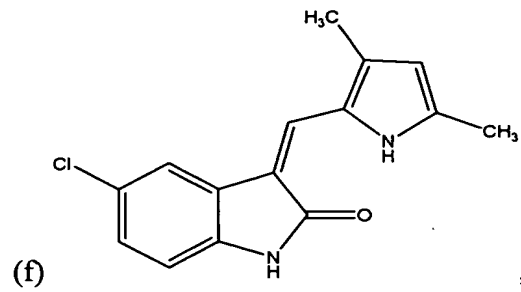
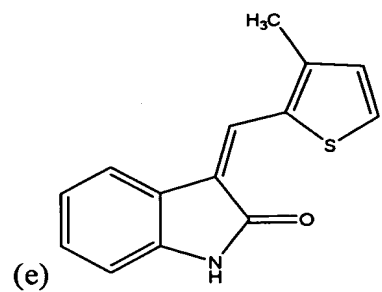
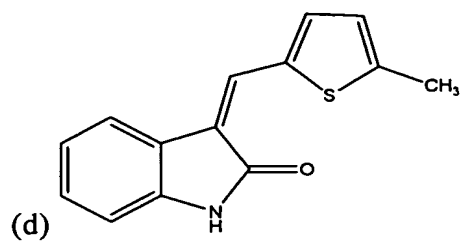
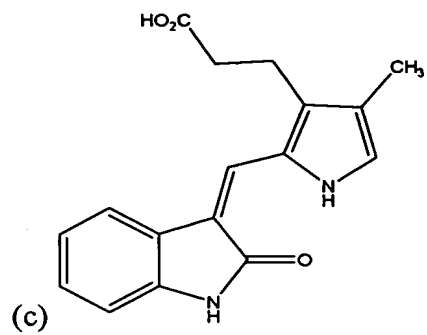
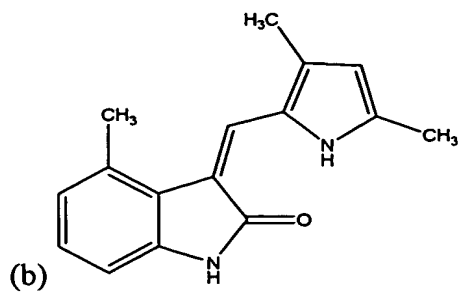
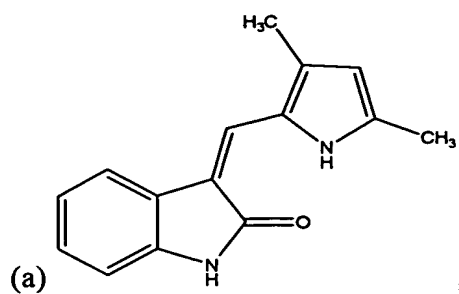
4. (Cancelled)

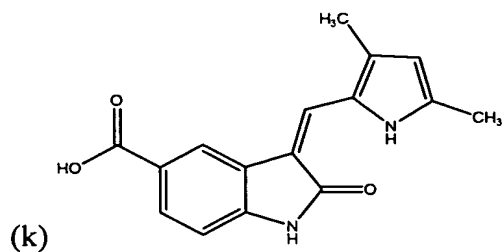
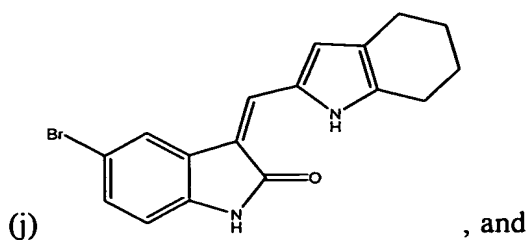
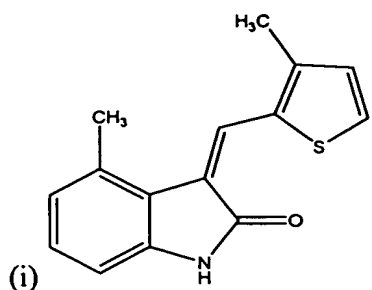
5. (Cancelled)

6. (Currently amended) The method of claim 51, wherein said receptor involved in angiogenesis is selected from the group consisting of Flt-1 and Flk-1.

7. (Cancelled)

8. (Currently amended) The method of claim 71, wherein said indolinone compound is selected from the group consisting of:





9. (Original) The method of claim 1, wherein said marker is present in a sample obtained from said subject.

10. (Original) The method of claim 9, wherein said sample is selected from the group consisting of whole blood, a blood fraction, blood plasma, blood serum, cells isolated from blood, whole urine, a urine fraction, saliva, cells isolated from saliva, spinal fluid, amniotic fluids, and biopsy of endothelial cells.

11. (Original) The method of claim 10, wherein said sample comprises monocytes.

12. (Cancelled)

13. (Cancelled)

14. (Cancelled)

15. (Cancelled)

16. (Original) The method of claim 1, wherein said marker is selected from the group consisting of DNA, RNA, mRNA, and protein.

17. (Cancelled)

18. (Currently amended) The method of claim ~~17~~1, wherein ~~said presence or~~ the amount of said marker is detected using an antibody.

19. (Withdrawn) The method of claim 17, wherein said presence or amount of said marker is determined by measuring blood clotting.

20. (Withdrawn) The method of claim 1, wherein said step of monitoring a marker related to angiogenesis comprises the step of determining the presence or amount of marker mRNA.

21. (Cancelled)

22. (Cancelled)

23. (Currently amended) The method of any one of claims ~~15-21~~16 or 18, wherein said marker is present in a sample obtained from athe subject.

24. (Cancelled)

25. (Cancelled)

26. (Cancelled)

27. (Withdrawn) The method of claim 1, wherein said marker is vascular endothelial growth factor mRNA.

28. (Currently amended) The method of claim 1, wherein said step of monitoring ~~the release of a marker is selected from the group consisting of~~ carried out by spectrophotometricalspectrophotometric determination after the addition of a specific chromogenic substrate, detection with antibodies, two stage clotting assay, one-stage recalcification assay, enzyme-linked immunosorbent assay, solid-phase enzyme immunoassay

employing polyclonal antisera, hydrogen peroxide assay, ~~and~~or measurement of tissue factor mRNA levels in endothelial cells.

29. (Cancelled)

30. (Cancelled)

31. (Previously presented) The method of claim 1, wherein said efficacious dose is between a minimal and a maximal dose.

32. (Withdrawn) The method of claim 1, wherein said marker is tissue factor.